

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION See paragraph 2 below

International application No.
PCT/EP2004/014000

International filing date (day/month/year)
09.12.2004

Priority date (day/month/year)
18.12.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/355, A61K31/4045, A61P43/00

Applicant
DSM IP ASSETS B.V.

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/014000

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. **type of material:**
 - a sequence listing
 - table(s) related to the sequence listing
 - b. **format of material:**
 - in written format
 - in computer readable form
 - c. **time of filing/furnishing:**
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,
 claims Nos. 10-13 (ia)

because:

the said international application, or the said claims Nos. - relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):
 the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for the whole application or for said claims Nos.
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

has not been furnished
 does not comply with the standard

the computer readable form

has not been furnished
 does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/014000

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|-------------------------------|-------------|-----------------------|
| Novelty (N) | Yes: Claims | 1-5, 10-13 |
| | No: Claims | 6-9 |
| Inventive step (IS) | Yes: Claims | 1-5, 10-13 |
| | No: Claims | 6-9 |
| Industrial applicability (IA) | Yes: Claims | 1-13 (see sep. sheet) |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)
and / or
2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/014000

Section III:

Claims 10-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Section V:

Reference is made to the following documents:

- D1: US 20020061870
- D2: WO 9720555
- D3: WO 9808490
- D4: DE 19939921
- D5: abstract of JP 2000143546
- D6: WO 9737670
- D7: abstract of JP 10029934

1. D1 describes a pharmaceutical composition comprising melatonin and vitamin E (p. 18, Table I) used to treat hearing conditions.
- D2 describes a pharmaceutical composition comprising melatonin and vitamin E (p. 10, I. 25, 26) used to treat anoxic or ischemic brain injury.
- D3 describes a pharmaceutical composition comprising melatonin and vitamin E polyethyleneglycol succinate/polyvinylpyrrolidone (p. 21, Ex. 8).
- D4 describes a pharmaceutical composition comprising melatonin and vitamin E (col. 3, ex. 1) used to slow down ageing process.
- D5 describes a pharmaceutical composition comprising melatonin and vitamin E wherein the latter is used as an antioxidant.
- D6 describes a tablet comprising 3 mg of melatonin and 125 IU of vitamin E used to treat magnesium deficiencies (P. 14, Table 3).
- D7 describes a plaster comprising melatonin and vitamin E.

The subject-matter of claims 6 or 8 is not novel in view of D1 to D7 and that of claim 9 neither in view of D6.

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2. None of the available prior art discloses or suggests that vitamin E has a beneficial effect on circadian rhythm.

Such subject-matter is thus novel and inventive (claims 1 to 5, 10 to 13).

3. For the assessment of the present claims 10-13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 to D7 is not mentioned in the description, nor are these documents identified therein.

Section VI:

Depending on the validity of the priority of the present application, US 2004/0034030 could be used as a novelty-destroying document with respect to claims 6-8 (p. 32, Table 1).